

REMARKS

Claim 2 was pending. Claims 1-8 are canceled herein, and new claims 9-23 are added. Support for the new claims are found throughout the specification in, *inter alia*, the originally filed claims and the specification at page 7, lines 14-22. Therefore it is believed that no new matter has been added.

Claims 9-23 are pending. No claim is allowed.

Formal matters

Applicants acknowledge the finality of the restriction requirement made by the Examiner and the Examiner's acknowledgement of the priority date claimed by Applicants.

The title is amended herein to more specifically reflect the contents of the disclosure.

The Examiner objected to the sequence disclosures in the specification. A substitute specification is provided herewith to identify all disclosed sequences by their sequence identifier.

The Examiner also objected to the specification because it contains an embedded hyperlink. The substitute specification provided herewith is amended to remove all embedded hyperlink and/or other form of browser-executable code.

The Examiner objected to claim 2 as being drawn to non-elected subject matter. Claim 2 is canceled herewith and rewritten as new claims 9-23.

In view of the above, Applicants believe the objections are overcome and respectfully request their withdrawal.

Rejection Under 35 U.S.C. § 101

Claim 2 is rejected under 35 U.S.C. § 101 as allegedly lacking a specific and substantial utility or a well established utility. According to the Examiner, the specification does not teach an function or biological activity for human OX2, *i.e.*, CD200, or its receptor, *i.e.*, OX2RH1.2 or CD200R. The Examiner asserts that claim 2 encompasses a large number of polypeptides that share

sequence homology with segments of SEQ ID NO:20 but may have different functions. Applicants traverse this rejection.

Applicants respectfully submit that the specification discloses a specific and substantial utility for the claimed binding compound of claims 9-23. The claimed binding compound binds the human CD200 receptor encoded by SEQ ID NO:20 or a fragment thereof. The specification discloses multiple specific and substantial utilities for CD200R, and thus for antibodies that bind CD200R. For example, the specification discloses a use for antibodies binding CD200R in the treatment of conditions where modulation of function of myeloid lineage cells is desirable. *See* the specification at, *e.g.*, page 74, lines 30-35. The specification identifies a number of embodiments where modulation of CD200R would be desirable such as

autoimmunity; an inflammatory condition; tissue specific autoimmunity; degenerative autoimmunity; rheumatoid arthritis; atherosclerosis; multiple sclerosis; vasculitides; delayed hypersensitivities; skin grafting; a transplant; spinal injury; stroke; neurodegeneration; or ischemia.

See the specification at page 75, lines 22-26. Each of these uses is a specific and substantial utility as these diseases involve or result from inappropriately activated macrophages, *i.e.*, cells of the myeloid lineage. It is readily apparent to one of skill in the art the usefulness of agents that can modulate the activation of macrophages in such disease states to ameliorate or mitigate symptoms of such diseases, and therefore the asserted utility is also credible.

Objective evidence supports the disclosed utility for CD200R and antibodies that bind this molecule. The ligand for this receptor is CD200, a cell bound antigen whose absence in mice, *i.e.*, CD200 $-/-$ mice, results in increased numbers of activated macrophages and a profound increase in susceptibility to autoimmune diseases affecting the brain and joint. *See, e.g.*, Hoek et al., *Science* 290:1768 (2000). Other studies demonstrate the ability of CD200R modulators to mitigate autoimmune disease and transplant rejection in animal models, each a utility disclosed in the specification. *See, e.g.*, Gorczynski et al., *Clin. Immunol.* 104:256-64 (2002) (showing the ability of CD200Fc to ameliorate collagen-induced arthritis in mice) and Gorczynski et al., *Eur. J. Immunol.* 31:2331-7 (2001) (showing that anti-CD200R antibody elicits immunosuppression, permitting increased allograft survival in mice). Moreover, recent evidence confirms that signaling through the

human CD200R downregulates macrophage activation in the manner predicted by the multitude of murine and rat studies involving CD200/CD200R interactions. *See, e.g.*, Exhibit B.

In sum, the utilities disclosed in the specification are specific to CD200R and substantial in the value of treating specific disease states and/or symptoms. Moreover, the objective post-filing evidence provides unquestionable credibility for the asserted utilities.

Accordingly, it is believed this basis for rejection may be withdrawn.

Rejection Under 35 U.S.C. § 112, first paragraph - written description

Claim 2 is rejected under 35 U.S.C. § 112, first paragraph as allegedly lacking sufficient written description. The Examiner asserts the claimed invention encompasses a potentially large genus of binding compounds against a large number of related polypeptides. Applicants traverse this rejection.

Applicants respectfully submit that the claimed invention as now claimed is drawn to binding compounds that specifically bind a polypeptide comprising SEQ ID NO:20 or fragments thereof. As this sequence is fully disclosed, the specification provides adequate written description for the claimed compounds.

Accordingly, it is believed this basis for rejection may be withdrawn.

Rejection Under 35 U.S.C. § 112, first paragraph - enablement

Claim 2 is rejected under 35 U.S.C. § 112, first paragraph as allegedly lacking reasonable enablement for the claimed invention. The Examiner alleges that the claims encompass potentially a large number of proteins of different structure or function which may or may not be an OX2 receptor. According to the Examiner, the prior art is silent on the structure and function of the OX2 receptor. Applicants traverse this rejection.

Applicants respectfully submit that the claimed invention as now claimed is drawn to binding compounds that specifically bind a polypeptide comprising SEQ ID NO:20 or fragments thereof. Applicants note that there is no legal requirement requiring certain proof of the function of the claimed polypeptide, *i.e.*, a working example, if the specification discloses at least one method for making and using the claimed invention. *See* MPEP § 2164.02. Applicants disclose the complete target sequence for the human OX2 receptor (CD200R) and method of making and using

binding compounds that bind the receptor. Nothing more is required to satisfy the enablement prong of 35 U.S.C. § 112, first paragraph.

Accordingly, it is believed this basis for rejection may be withdrawn.

Rejection Under 35 U.S.C. § 112, second paragraph

Claim 2 is rejected under 35 U.S.C. § 112, second paragraph as allegedly being indefinite. According to the Examiner, claim 2 is indefinite because it is unclear whether limitations within the claim are in the alternative or in combination. The Examiner asserts that the term “a natural sequence primate OX2RH1.2 polypeptide is indefinite because it is unclear what composition is being referred to. The Examiner also asserts that the limitation “a natural OX2RH polypeptide of claim 1” of claim 2 has insufficient antecedent basis. Applicants traverse this rejection.

Applicants believe the new claims provided herein render these rejections moot as the cited terms are not employed and the limitations are now contained in dependent claims.

Accordingly, it is believed this basis for rejection may be withdrawn.

Rejection Under 35 U.S.C. § 102 (b)

Claim 2 is rejected under 35 U.S.C. § 102 (b) as allegedly being anticipated by Preston et al. The Examiner states that claim 2 is drawn to a binding compound comprising an antigen binding site from an antibody which specifically binds to a natural OX2RH polypeptide, wherein the OX2RH is from a rodent. According to the Examiner, Preston discloses a monoclonal antibody that specifically binds OX2 ligand on macrophages, and an antibody used to clone the OX2 receptor, OX102, also bound macrophages. The Examiner asserts that both antibodies bind specifically to the same surface molecule of peritoneal macrophages, and MRC OX88 antibody is an antibody that binds specifically to a natural rodent OX2 ligand/receptor polypeptide. The Examiner acknowledges the identity of the murine OX2 ligand is unknown. Thus, the Examiner argues that Preston discloses the instant invention. Applicants traverse this rejection.

Applicants submit that Preston fails to anticipate the instant invention because it fails to teach each and every element of the claimed invention. Preston lacks any disclosure regarding the sequence or identity of the human OX2/CD200 receptor. The claimed binding compounds binds a

specific sequence or a fragment thereof of the human CD200 receptor. Preston is completely silent regarding the sequence of any OX2 receptor, much less the human receptor.

Accordingly, it is believed this basis for rejection may be withdrawn.

CONCLUSION

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding objections and rejections and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark Office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. 03-1952 referencing docket no. 140942000900. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

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Respectfully submitted,

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